Br J Vener Dis 1984;**60**:204-6

Correspondence

TO THE EDITOR, *British Journal of Venereal Diseases*

Failure of pirampicillin in treating chlamydial infections

Sir,

It has hitherto been customary to use ampicillin in the treatment of acute salpingitis and acute epididymitis. In recent years it has become clear that *Chlamydia trachomatis* infection may be an important factor in these diseases,[1] [2] but to our knowledge no report on the efficacy of ampicillin in the treatment of chlamydial infections has been published, although the in vitro activity of ampicillin against *C trachomatis* (MIC 0·25 mg/l) indicates possible efficacy.

We treated 15 patients who had chlamydia positive non-gonococcal urethritis with pivampicillin (500 mg by mouth three times daily for seven days), pivampicillin being an ampicillin which is almost completely absorped. Urethral specimens were cultured for *C trachomatis* on days 10 and 17 after the start of treatment. Of the 14 patients who completed the study, seven became chlamydia negative, while seven still harboured *C trachomatis* in the urethra. Of the seven treatment failures, three were negative at the first follow up, while in two only one inclusion was found in the cell cultures, probably indicating suppression of the infection. All seven were positive at the second follow up, but denied the possibility of reinfection.

The results are unfavourable when compared with the effect of tetracyclines and erythromycin in similar treatment regimens.[4] The role of *C trachomatis* in the aetiology of acute salpingitis and acute epididymitis necessitates a re-examination of present treatment guidelines. In addition, the frequent association of *C trachomatis* and *Neisseria gonorrhoeae* should influence the choice of treatment for gonococcal disease.

Yours faithfully,

*Hans Hagdrup**
*Johannes Kristensen**
Jens Scheibel†

*Department of Dermatology and Venereology,
Rigshospital, Copenhagen, and
†Department of Medical Microbiology,
University of Copenhagen, Denmark

References

1. Berger RE, Alexander ER, Harnisch UP, *et al.* Etiology, manifestations and therapy of acute epididymitis. *J Urol* 1971;**127**:750-4.
2. Paavonen J, Saiku P, Vesterinen E, Aho K. *Chlamydia trachomatis* in acute salpingitis. *Br J Vener Dis* 1979;**55**:203-6.
3. Ridgway GL, Owen JM, Oriel JD. The antimicrobial susceptibility of *Chlamydia trachomatis* in cell culture. *Br J Vener Dis* 1978;**54**:103-6.
4. Johannisson G. Studies on *Chlamydia trachomatis* as a cause of lower urogenital tract infection. *Acta Derm Venereol [suppl] Stockh* 1981;**93**:1-55.

TO THE EDITOR, *British Journal of Venereal Diseases*

Herpes Vaccine

Sir,

Considerable publicity has recently been given to the Ac NFU_1 (S^-) MRC herpes vaccine for the prevention of genital herpes. The scientific evidence to support the efficacy of this preparation is, however, extremely limited. During the past nine months the *British Journal of Venereal Diseases* has carried two articles about drug trials with the vaccine.[1] [2] The first considered a vaccination programme in consorts of patients with herpes, and the only controls were patients seen at the clinic before the vaccination programme. No attempt was made to show that the groups were similar in regard to the number of patients with primary or recurrent infection, the viral type, the antibody status of patients and consorts, or the frequency and type of sexual activity. In addition the "control" group consisted of only 20 patients, whereas the treatment group contained 60 patients. The authors made no attempt to analyse the results statistically.

The second study considered a vaccination programme in patients who had suffered a first attack of herpes. Historical controls were used from the same department and also from a sexually transmitted disease (STD) clinic at another centre. No attempt was made to show that the groups were similar in regard to age, sex, severity of the first attack, and antibody status. In addition 38% of all isolates were not typed. The authors did not state how long after the first episode patients were vaccinated or if the initial examination was given at the same time in all patients. As in the first study, no attempt was made to analyse the results statistically.

The authors dismiss viral type as a possible explanation for the difference in rates of recurrence between vaccinated and control patients, and referred to our work to argue this point. However they misquoted and misrepresented the work of the Middlesex Hospital. The correct information is as follows: five (45%) out of 11 Type I patients compared with 14 (82%) of 17 Type II patients had recurrences at six months following treatment in a double blind placebo controlled randomised study of intravenous acyclovir ($p<0·05$). At 12 months all Type II and 59% of the Type I patients had had recurrences ($p<0·02$).[3] Corey *et al* in a long term follow up study of untreated patients in Seattle have confirmed that patients with Type II infection have recurrences more frequently than those with Type I.[4]

A final aspect of these studies that warrants consideration is the possibility that vaccination may enhance subclinical infection, thus increasing the possibility that vaccinated patients may transmit the disease without knowing it. In neither of the two studies were patients screened to assess asymptomatic viral shedding. The only way to assess whether vaccination has any effect in preventing or modifying genital herpes is to conduct double blind randomised placebo controlled studies. Until such studies are undertaken the clinical efficacy of the Birmingham vaccine remains completely unproved.

Finally, it should be pointed out that the vaccine does not have a product licence from the Committee on Safety of Medicines (CSM), and patients should be discouraged from being vaccinated until the manufacturers have obtained such a licence.

Yours faithfully,

A Mindel

Academic Department of
Genitourinary Medicine,
The Middlesex Hospital Medical School,
London

References

1. Skinner GRB, Woodman CBJ, Hartley CE, *et al.* Preparation and immunogenicity of vaccine Ac NFU_1 (S^-) MRC towards the prevention of herpes genitalis. *Br J Vener Dis* 1982;**58**:381-6.
2. Woodman CBJ, Buchan A, Fuller A, *et al.* Efficacy of vaccine Ac NFU_1 (S^-) MRC 5 given after an initial clinical episode in the prevention of herpes genitalis. *Br J Vener Dis* 1983;**59**:311-3.

3. Mindel A, Sutherland S. Genital herpes: the disease and its treatment including intravenous acyclovir. *J Antimicrob Chemother* 1983; **12** suppl: 51-9.
4. Corey L, Adams HG, Brown ZA, Holmes KK. Genital herpes simplex virus infections: clinical manifestations course and complications. *Ann Int Med* 1983; **98**: 958-72.

TO THE EDITOR, *British Journal of Venereal Diseases*

Anal smear test to diagnose occult anorectal infection with human papillomavirus in men

Sir,

Infection of the female genital tract with human papillomavirus (HPV) has assumed increasing importance since the cytological recognition of an occult form (non-condylomatous) indicated that its true prevalence is much higher than previously suspected.[1 2] Indeed its role as a possible aetiological agent (or co-factor) in the development of cervical, vulval, and vaginal squamous cell carcinoma has been postulated.[3] Recent identification of deoxyribonucleic acid (DNA) sequences of herpes simplex virus (HSV) subtypes in tumours [4] (Zur Hausen H, personal communication) and of humoral markers in serum [5] of patients with cervical cancer have lent credence to the hypothesis. The biology of tumour development has not been ascertained, although association with recognised oncogenic "permissive" factors of immune deficiency in kidney transplant recipients has been described.[6]

Recent demonstration of the acquired immune deficiency syndrome (AIDS) and lesser immunosuppression in homosexual men, and the associated instances of viral opportunism in this group,[7] the high incidence of HSV,[8] and the knowledge that condylomata are common, have led us to initiate a study to determine the incidence of non-condylomatous HPV infection of the anal canal by cytological means. Sporadic cases of anorectal cancer in homosexual men, occurring in a younger age group than usual, have been described, and the worldwide increasing incidence and mortality of invasive squamous cell cancer in young women (under 40 years) [9 10] (often with an explosive course) would lead us to expect a possible similar increase in this group of men, 30-40% of whom may have some form of immune deficiency.[7]

To assess the feasibility of simple cytological diagnosis of occult anorectal HPV infection, we studied 102 homosexual men, aged 20 to 85 (mean age 32, median age 28). Anal smears were taken under proctoscopic vision from the level of the dentate line, processed in the same manner as routine Papanicolaou smears from women, and were all reviewed by me. Cytodiagnosis of HPV infection in smears from men presents morphological differences from those from women (Medley G and Drake M, unpublished observation). The finding of a transformation zone (squamocolumnar junction), however, with the capacity for metaplastic change, suggests, and can be shown to have, a possible vulnerability to development of dysplastic or precancerous change akin to the cervical transformation zone.

The results of the study are given in the table. Of 102 patients, 45 (44%) had features of HPV infection. Many had previously had surgical or medical treatment for external anal condylomata, and a few still had them (two of the men with features of HPV infection and three of those without. This study will form the nucleus of a much larger prospective investigation and all patients will have documentation of current immunological status by customary protocol for such investigations, and be assessed both immunologically and cytologically at six monthly intervals. I thus hope to monitor the behaviour of this infection in a potentially immunocompromised group, and learn more of the biology of viral oncogenesis, if in fact this is a true hazard of this disease.

	Patients (n = 102)	*Smears (n = 111)*
HPV infection without atypia	18	20
HPV infection with minor warty atypia	16	19
HPV infection with mild or moderate dysplasia (CIN 1 or 2*)	11	14
Total HPV infection	45	53
Non-specific inflammatory changes	16	16
No features of HPV infection	41	42

*Cervical intraepithelial neoplasia I or II

I am deeply indebted to Dr Rex Melville who took the smears, without whose skill and care the study would have been impossible.

Yours faithfully,

Gabriele Medley

Department of Anatomical Pathology,
Prince Henry's Hospital and Victorian Cytology (Gynaecological) Service,
Melbourne, Australia

References

1. Meisels A, Fortin R. Condylomatous lesions of the cervix and vagina. *Acta Cytol* 1976; **20**: 505-9.
2. Laverty CR, Russell P, Hill E, Booth N. The significance of non-condylomatous wart virus infection of the cervical transformation zone. *Acta Cytol* 1978; **22**: 195-201.
3. Zur Hausen H. Condylomata acuminata and human genital cancer. *Cancer Research* 1976; **36**; 794.
4. Kurman J, Bennett-Jenson A, Lancaster W. Papilloma virus infection of the cervix II. *Am J Surg Pathol* 1983; **7**: 39-52.
5. Baird PJ. Serological evidence for the association of papilloma virus and cervical neoplasia. *Lancet* 1983; ii: 17.
6. Schneider V, Kay S, Lee HM. Immunosuppression as a high risk factor in the development of condyloma acuminatum and squamous neoplasia of the cervix. *Acta Cytol* 1983; **27**: 220-4.
7. Pinching AJ, Jeffries DJ. Donaghy M. Studies of cellular immunity in male homosexuals in London. *Lancet* 1983; ii: 126.
8. Goodell SE, Quinn TC, Mketichian E, *et al.* Herpes simplex virus proctitis in homosexual men. *N Engl J Med* 1983; **308**: 868-71.
9. Armstrong B, Holman D. Increasing mortality from cancer of the cervix in young Australian women. *Med J Aust* 1981; **1**: 460-2.
10. Canadian Task Force. Report on cervical cancer screening programs. *Can Med Assoc J* 1982; **127**: 581.
11. Medley, G., Drake M. Cytological diagnosis of anorectal HPV infection. (To be published).

TO THE EDITOR, *British Journal of Venereal Diseases*

Buschke-Loewenstein tumour and laser treatment

Sir,

We read with great interest the article of Harvey, Glen, and Watson entitled "Buschke-Loewenstein tumour of the penis" which was recently published in the *British Journal of Venereal Diseases*.[1] The authors described a 30 year old married man with giant condylomata acuminata of the penis which were treated by subtotal amputation of the penis. In the article the authors stated: "Laser treatment would have required an experienced operator; although it has been used in simple condylomata acuminata, it would not have been easy to assess the depth of the tumour."